UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte KENNETH S. POLONSKY, YUKIO HORIKAWA, NAOHISA ODA, NANCY J. COX, KENICHI OTANI, CRAIG L. HANIS, GRAEME I. BELL, SEAMUS KEVIN SREENAN, and YUN-PING ZHOU

Appeal No. 2005-0258
Application No. 09/768,877

ON BRIEF[1]

Before ELLIS, ADAMS, and GREEN Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 18-21, 49-51, 53-64, 115 and 116. Of the remaining pending claims, claims 65-113 have been withdrawn from consideration, and claims 52 and 114 stand objected as depending from a rejected claim.[2]

[1] Appellants waived their request for oral hearing. Paper received February 23, 2005. Accordingly, we considered this appeal on Brief.

[2] The objection to claims 52 and 114 is the subject matter of a petition and is not properly before us on appeal. Accordingly, we have not considered claims 52 and 114 in our deliberations.

Claims 51 and 53 are illustrative of the subject matter on appeal and are reproduced below:

51. A method of screening for a modulator of calpain 10 function comprising:
    a) obtaining an [sic] calpain 10 polypeptide;
    b) contacting the calpain 10 polypeptide with a putative modulator; and
    c) assaying for modulation of calpain 10 function by the putative modulator.

53. The method of claim 51, wherein the calpain 10 polypeptide has a sequence comprising amino acid 1 to 47 of SEQ ID NO:2[.]

The references relied upon by the examiner are:

Van De Loo et al. (Van de Loo), "An oleate 12-hydroxylase from Ricinus communis L. is a fatty acyl desaturase homolog," Proc. Natl. Acad. Sci. USA, Vol. 92, pp. 6743-6747 (1995)

Meyer et al. (Meyer), "Biologically active monomeric and heterodimeric recombinant human calpain I produced using the baculovirus expression system," Biochem. J., Vol. 314, pp. 511-519 (1996)

Broun et al. (Broun), "Catalytic Plasticity of Fatty Acid Modification Enzymes Underlying Chemical Diversity of Plant Lipids," Science, Vol. 282, pp. 1315-1317 (1998)

Witkowski et al. (Witkowski), "Conversion of a ß-Ketoacyl Synthase to a Malonyl Decarboxylase by Replacement of the Active-Site Cysteine with Glutamine," Biochemistry, Vol. 38, pp.11643-11650 (1999)

Bork, "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle," Genome Research, Vol. 10, pp. 398-400 (2000)

Seffernick et al. (Seffernick), "Melamine Deaminase and Atrazine Chlorohydrolase: 98 Percent Identical but Functionally Different," J. Bacteriol., Vol. 183, No. 8, pp. 2405-2410 (2001)

GROUNDS OF REJECTION

I. Claims 18-21, 49-51, 53-64, 115 and 116 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite in the recitation of the term "calpain 10."

II. Claims 19, 49 and 53 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification fails to adequately describe the claimed invention.

III. Claims 18-21, 49-51, 53-64, 115 and 116 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification fails to adequately describe the claimed invention.

IV. Claims 18-21, 49-51, 53-64, 115 and 116 stand rejected under 35 U.S.C. § 112, first paragraph, as based on an insufficient disclosure to support or enable the scope of the claimed invention.

We reverse rejections I and II. We affirm rejection III. Having affirmed the rejection of all claims under the written description provision of 35 U.S.C. § 112, first paragraph, we do not reach the merits of rejection IV.

DISCUSSION

Definiteness:

Claims 18-21, 49-51, 53-64, 115 and 116 stand rejected under 35 U.S.C. § 112, second paragraph. As we understand the examiner's rejection, the scope of the claimed invention is open to include a method of screening for a modulator of the function of any "calpain 10" of any structure from any organism and therefore "one of skill in the art cannot [be] reasonably apprised of the scope of the invention." Answer, page 6. In response appellants assert (Brief, page 12), "[t]he breadth of a claim should not be equated with indefiniteness."

We agree. In re Gardner, 427 F.2d 786, 788, 166 USPQ 138, 140 (CCPA 1970) ("[b]readth is not indefiniteness."). In our opinion, a person of ordinary skill in the art reading appellants' claimed invention in light of their specification would understand that the claims are open to include a method of screening for a modulator of the function of any "calpain 10" of any structure[3] from any organism. Accordingly, we reverse the rejection of claims 18-21, 49-51, 53-64, 115 and 116 under 35 U.S.C. § 112, second paragraph.

New Matter:

Claims 19, 49 and 53 stand rejected under 35 U.S.C. § 112, first paragraph.[4] According to the examiner (Answer, page 6), "[t]his is a new matter rejection." In this regard, the examiner finds (Answer, bridging paragraph, pages 6-7), claims 19, 49 and 53

> encompass a method of screening for a modulator of calpain 10 function wherein the calpain 10 polypeptide used comprises amino acids 1-47 of SEQ ID NO: 2. While the specification discloses a method as described above wherein the calpain 10 polypeptide used is that of SEQ ID NO: 2, the Examiner has been unable to locate adequate support in the specification for a method of screening for a modulator of calpain 10 function with a calpain 10 polypeptide which comprises specifically amino acids 1-47 of SEQ ID NO: 2. Furthermore, the Examiner has not been able to find a specific reference to amino acids 1-47 of SEQ ID NO: 2. Thus there is no indication that methods using specifically calpain 10 polypeptides which comprise amino acids 1-47 of SEQ ID NO: 2

[3] We note, however, that claims 19, 49, 50, and 53 limit the structure of the calpain 10 polypeptide by requiring that "the calpain 10 polypeptide comprises amino acid 1 to 47 of SEQ ID NO:2." In addition, we note that claims 115 and 116 limit the source of the calpain 10 polypeptide to a human calpain 10.

[4] As we understand the examiner's rejection, claim 49 was included in the rejection because it depends from claim 19. We note, however, that claim 50, depends from claim 49. Accordingly, it is unclear why claim 50 was not also included in this rejection.

were within the scope of the invention as conceived by Appellants at the time the application was filed.

We note that the recitation -- "amino acids 1-47 of SEQ ID NO:2" -- was not part of the originally filed claims. Instead, this limitation was added to claims 19 and 53 in the amendment filed January 21, 2003.

In response, appellants assert (Brief, page 13), "[t]he phrase 'amino acids 1-47 of SEQ ID NO:2' is described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention." Specifically, appellants direct our attention to page 29, line 24 of their specification wherein exon 1 of calpain 10 is described as "Exon 1 nt 1235-1515 (cds 1375-1515)," wherein the abbreviation "nt" stands for nucleotide positions relative to SEQ ID NO:1. Id. According to appellants (Brief, bridging paragraph, pages 13-14), "one of ordinary skill in the art would recognize that the coding region of exon 1, which is set forth in SEQ ID NO:1 and encodes the exemplary polypeptide of SEQ ID NO:2, corresponds to the amino acids 1-47 of calpain 10."

The examiner agrees (Answer, page 19) that the nucleotide sequence of exon 1 as disclosed on page 29 of appellants' specification encodes amino acids 1-47 of SEQ ID NO:2. The examiner, however, finds (id.), "[a]ppellants have not indicated which section of the specification discloses practicing the claimed method with a polypeptide comprising amino acids 1-47 of SEQ ID NO:2 as a preferred embodiment."

We disagree. According to appellants' specification (page 30), "[t]here are a number of calpain 10 isoforms that result from alternative splicing of the

CAPN10 gene. Alternative splicing generates eight related but structurally distinct proteins." These eight proteins are identified as CALPAIN 10a, 10b, 10c, 10d, 10e, 10f, 10g and 10h. See Table 1, specification, page 30. As set forth in Table 1, all eight proteins comprise exon 1. As discussed above, exon 1 encodes amino acids 1-47 of SEQ ID NO:2. In the "summary of the invention" section of appellants' specification (page 7), appellants disclose that "the invention relates to methods of screening for modulators of calpain function comprising the steps of: a) obtaining an [sic] calpain polypeptide." On page 8 of the specification, appellants disclose

> [t]he invention also relates to isolated and purified calpain 10 polypeptides, for example, polypeptides forming calpain 10a, calpain 10b, calpain 10c, calpain 10d, calpain 10e, calpain 10f, calpain 10g, [and] calpain 10h.... Such polypeptides may have an amino acid sequence as set forth in any of SEQ ID NO:2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, [and] SEQ ID NO: 16....

Table 1 at page 30 of appellants' specification discloses that SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14 and 16 correspond to calpain 10a, 10b, 10c, 10d, 10e, 10f, 10g, and 10h respectively.

For the foregoing reasons we reverse the rejection of claims 19, 49 and 53 under 35 U.S.C. § 112, first paragraph.

Written Description:

Claims 18-21, 49-51, 53-64, 115 and 116 stand rejected under the written description provision of 35 U.S.C. § 112, first paragraph. At page 7 of the Brief, appellants state "[c]laims 18-21, 49-51 and 53-64 do not stand or fall with the other claims...." In addition, appellants state (id.), "claims 19 and 53, stand or fall separately from claims 18, 20, 21, 49, 51, 54-55, and 57-60...." As we understand appellants' statements the claims stand or fall together in the following two groups:

I. Claims 18, 20, 21, 49, 50, 51, 52, 54, 55, 57-64, 115 and 116; and

II. Claims 19 and 53.

However, we find no separate arguments as to the claims or designated groups as required by 37 CFR § 1.192(c)(7) (2002) (Claims stand or fall together "unless a statement is included that the claims of the group do not stand or fall together and, in the argument under paragraph (c)(8) of this section, appellant explains why the claims of the group are believed to be separately patentable. Merely pointing out differences in what the claims cover is not an argument as to why the claims are separately patentable." (Emphasis added)). Therefore, the claims on appeal are considered to stand or fall together.

Since all claims stand or fall together, we limit our discussion to representative independent claim 51. Claims 18-21, 49, 50, 53-64, 115 and 116 will stand or fall together with claim 51. In re Young, 927 F.2d 588, 590, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991).

According to the examiner (Answer, page 8, emphasis removed),

> [o]nly one human and one mouse gene have been disclosed as encoding calpain 10 polypeptides and only two completely functional calpain 10 polypeptides have been disclosed. The specification fails to provide the structures of all the calpain 10 polypeptides ... [encompassed by] the claimed method, or the structural elements which are common to all calpain 10 proteins from any organism. In addition, the specification fails to disclose ... the critical structural elements in the human and mouse calpain 10 polypeptides disclosed which are required in any polypeptide to display calpain 10 activity.

As we understand it, the method of claim 51 is open to the use of a calpain 10 polypeptide of any structure from any source. Therefore, the method of claim 51 reads generically on the use of any calpain 10 polypeptide from any source. Thus, the specification must adequately describe the genus of calpain 10 polypeptides encompassed by the method of claim 51. As a matter of logic, a method of using a product cannot be adequately described without describing the product. For the following reasons, we agree with the examiner that the specification does not adequately describe this genus of calpain 10 polypeptides.

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997), provides the appropriate analysis. The claims in Lilly were directed generically to vertebrate or mammalian insulin cDNAs. See id. at 1567, 43 USPQ2d at 1405. The court held that a structural description of a rat cDNA was not an adequate description of these broader classes of cDNAs, because a "written description of an

invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name, ' of the claimed subject matter sufficient to distinguish it from other materials." Id. (bracketed material in original).

The Lilly court explained that

> a generic statement such as. . . 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus.

Id. at 1568, 43 USPQ2d at 1406. Finally, the Lilly court set out exemplary ways in which a genus of cDNAs could be described:

> A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

Id.

Our appellate reviewing court revisited the issue of describing DNA. See Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court held that a claimed DNA could be described without, necessarily, disclosing its structure. The court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties,

functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" See id. at 1324, 63 USPQ2d at 1613 (emphasis omitted, ellipsis and bracketed material in original).

Post-Lilly, the court has clarified that the representative species need not necessarily be described in terms of their complete chemical structure. See Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 964, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002) ("[T]he written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" (emphasis omitted, alterations in original)).

Our appellate review court has also noted that "Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." Amgen, Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1332, 65 USPQ2d 1385, 1398 (Fed. Cir. 2003).

This standard applies to polypeptides as well as DNAs. See University of Rochester v. G.D. Searle & Co., Inc., 358 F.3d 916, 925, 69 USPQ2d 1886, 1893 (Fed. Cir. 2004) ("We agree with Rochester that Fiers, Lilly, and Enzo differ from this case in that they all related to genetic material whereas this case does

not, but we find that distinction to be unhelpful to Rochester's position. It is irrelevant; the statute applies to all types of inventions. We see no reason for the rule to be any different when non-genetic materials are at issue.").

In this case, the examiner finds (Answer, page 8, emphasis removed), "[o]nly one human and one mouse gene have been disclosed as encoding calpain 10 polypeptides...." According to the examiner (id.), "the human calpain 10 polypeptides [(isoforms)] disclosed in the specification are splice variants encoded by a single gene, i.e. CAPN10." Therefore, as we understand the examiner's argument (Answer, bridging sentence, pages 7-8), while appellants' specification discloses the complete primary structure (amino acid sequence) of a mouse and various isoforms of human calpain 10 polypeptide, produced by alternative splicing of a single human calpain gene, these species are insufficient to describe the entire genus of calpain 10 polypeptides encompassed by the method of claim 51.

In response, appellants assert (Brief, page 14) that they have disclosed "an exemplary full length of [sic] calpain 10 and its various exon regions that are differentially spliced to create different calpain 10 isomers." We recognize that there is no dispute on this record that appellants have disclosed a "full length" human calpain 10 polypeptide and various human calpain 10 isomers. We also recognize that appellants make no assertion on this record that sequences of other representative species of calpain 10 are disclosed in their specification. Accordingly, as we understand appellants' arguments the disclosure of the human calpain 10 polypeptide isoforms, when coupled with a correlation

between the function and structure of the calpain 10 polypeptide is sufficient to describe the entire genus of calpain 10 polypeptides encompassed by the method of claim 51. In this regard, appellants direct our attention to various portions of their specification and figures. We take each in turn.

Appellants direct our attention to Table 1, at page 30 which according to appellants (Brief, page 14), "describes the calpain 10 isoforms with indication as to the encoded exons, the polypeptide length and the sequences corresponding to the SEQ ID Nos." In addition, appellants direct our attention to figure 1, which appellants assert (id.), diagrams "the alternative spliced forms of calpain 10 indicating the various domains." At page 30 of appellants' specification, we note that appellants disclose

> [t]here are a number of calpain 10 isoforms that result from alternative splicing of the CAPN10 gene. Alternative splicing generates eight related but structurally distinct proteins. The structures of the mRNAs encoding each isoforms are defined by unique combinations of exons and splice donor and acceptor sites (see Table 1, FIG. 1).

As we understand it, the disclosure in Table 1 and Fig. 1 relate to human calpain 10 isoforms, which according to appellants are "structurally distinct proteins." Appellants provide no disclosure that all species encompassed by the method of claim 51 would be expected to contain similar splice variants of these structurally distinct proteins. Further, appellants stop short of stating that each isoform is expected to have the same or similar function. In this regard, we note that the examiner finds (Answer, page 8),

> [a]s it can be seen at least in Figure 1, not all the splice variants disclosed will have the same activity as that of the polypeptide of SEQ ID NO:2 (Figure 1A, calpain 10[a]) which is the complete gene

> product. See for example Figure 1H, where the polypeptide labeled calpain 10[h] lacks all the domains present in calpain 10[a] which correlate with the proteolytic activity associated with calpains and only contains domain I and domain T (C-terminal domain).

Regarding the calpain 10 domains, appellants assert (Brief, page 14), figure 5 provides "an alignment of calpain 10 and various calpains indicating the domains." Further, appellants assert (Brief, bridging sentence, pages 14-15), "a structural description of the domains of calpain 10, such as the specific calmodulin-like Ca^{2+} binding domain" is disclosed on page 31 of the specification.

At page 31 of their specification, appellants disclose that

> [c]alpain 10 diapain[5] is an atypical calpain and is similar in structural organization to the other atypical calpains, calpain 5 and calpain 6, in that it has domains I-to-III, lacks the calmodulin-like Ca^{2+}-binding domain and has a divergent C-terminal domain, domain T.... Calpains 5, 6 and 10 define a distinct subfamily (FIG. 6).

Accordingly, notwithstanding appellants' assertion to the contrary, calpain 10 does not contain a calmodulin-like Ca^{2+} binding domain. In addition, while

[5] According to appellants' specification (page 29), "[c]alpain 10 is a 'diapain' that has been identified by the present invention." With regard to the term "diapain", appellants' explain (specification, page 33), "[s]ince it is a variant in the calpain 10 gene that is associated with diabetes, the inventors suggest that the protein encoded by this gene be called diapain-1 (diabetes calpain). As such the terms 'calpain 10' and diapain-1 are used interchangeably herein." Accordingly, we note that the genus encompassed by the term "calpain 10" as it is used in the method of claim 18 also reads on variants associated with the calpain gene that are associated with diabetes.

appellants disclose that calpain 10 "has domains I-to-III" we note, as does the examiner (Answer, page 8), that several calpain 10 isoforms do not contain domains I-III. Specifically, with reference to figures 1A-1H, we note that calpains 10c, 10f, 10g and 10h appear to be missing all or part of domain III, and calpains 10f, 10g and 10h appear to be missing part of domain II. Regarding, domain T, calpains 10b, and 10c-10h appear to be missing all or part of domain T. In addition, as the examiner explains (Answer, page 8),

> while the specification discloses that a calpain 10 protein is similar in structure to calpain 5 and 6 (page 31, lines 8-11), it does not provide any guidance as to which ... structural elements ... are specific to a calpain 10 and are not found in a calpain 5 or 6 such that one of skill in the art would know if a polypeptide is a calpain 10 or a calpain 5 or 6.

Accordingly, we are not persuaded by appellants' assertion (Brief, page 15), "that calpains are a family of structurally related intracellular multidomain cysteine proteinases containing a papain-related catalytic domain, whose activity depends on calcium." Without a disclosure of the structural characteristics that distinguish calpain 10 from other members of the calpain family, there is no way to distinguish calpain 10 from the other members of the calpain family. As the examiner explains (Answer, page 8),

> [t]he specification fails to provide the structures of all the calpain 10 polypeptides required in the claimed method, or the structural elements which are common to all calpain 10 proteins from any organism. In addition, the specification fails to disclose which are the critical structural elements in the human and mouse calpain 10 polypeptides disclosed which are required in any polypeptide to display calpain 10 activity.

For the foregoing reasons, we disagree with appellants' assertion (Brief, page 15), "[g]iven the more than adequate description provided in the

specification and figures, it would be clear to one of skill in the art that the [a]ppellants had possession of the claimed invention at the time of filing sufficient to practice the invention." To the contrary, as we understand it, appellants had possession of the structurally-distinct calpains 10a-10h as diagrammatically illustrated in figures 1A-1H (SEQ ID NOs:2, 4, 6, 8, 10, 12, 14 and 16), and the mouse calpain 10 set forth in SEQ ID NO:18. See specification page 8. As the examiner points out (Answer, page 8), "[t]he genus of polypeptides ... [encompassed by] the claimed method is a large and structurally variable genus." The specification fails to provide any correlation between the structures of these structurally-distinct calpains and any functional activity. Accordingly, it is our opinion that the application does not describe structural features common to members of the genus, either expressly or via a known correlation between structure and function. The evidence of record supports the examiner's position that the description of calpain 10 polypeptides is inadequate to describe the full genus of calpain 10 polypeptides encompassed by claim 51.

While the inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to the instant claim. Claim 51 is directed to a method, rather than a product, but carrying out the claimed method requires the use of a calpain 10 polypeptide. In our opinion, the instant specification does not provide an adequate description of the genus of calpain 10 polypeptides encompassed by the method of claim 51, per Lilly, by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Nor does the specification

describe the genus by describing a "representative number" of calpain 10 polypeptides, wherein the representative species are described according to the standard of either Lilly or Enzo. Since the specification does not adequately describe the calpain 10 polypeptides required to practice the method of claim 51, it does not adequately describe the claimed method.

For the foregoing reasons, we affirm the rejection of claim 51 under the written description provision of 35 U.S.C. § 112, first paragraph. As discussed supra claims 18-21, 49, 50, 53-64, 115 and 116 fall together with claim 51.

Enablement:

Claims 18-21, 49-51, 53-64, 115 and 116 stand rejected under 35 U.S.C. § 112, first paragraph, as based on an insufficient disclosure to support or enable the scope of the claimed invention. Having disposed of all claims on appeal as unpatentable over the written description provision of 35 U.S.C. § 112, first paragraph, we do not reach the merits of the rejection under the enablement provision of 35 U.S.C. § 112, first paragraph.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Joan Ellis
Administrative Patent Judge

Donald E. Adams
Administrative Patent Judge

Lora M. Green
Administrative Patent Judge

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Gina N. Shishima
FULBRIGHT & JAWORSKI L.L.P.
Suite 2400
600 Congress Avenue
Austin TX 78701